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NUTRITION REVIEWS

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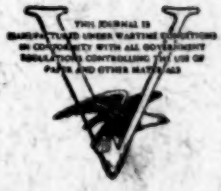

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FREDRICK J. STARE, Ph.D., M.D., Assistant Professor of Nutrition, Schools of Medicine and Public Health, Harvard University; Associate in Medicine, Peter Bent Brigham Hospital, Boston. Editorial Office, 25 Shattuck St., Boston, Mass.

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NUTRITION REVIEWS

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THE FOOD PROBLEMS OF BRAZIL

Until recently Brazilian scholars who sought a scientific explanation of our type of socio-economic evolution neglected entirely the nutrition problem. In the various theories of sociologic interpretation, all of the shortcomings of our civilization were attributed to climatic and racial factors. The nutrition factor was always neglected. Only in the last ten years, following stressing of the problem by Brazilian medical schools, has there been a general reaction in recognizing nutrition, and today our sociologists, cognizant of the researches carried out in this field, are unanimous in affirming that the country's inadequate nutrition has been a considerable handicap in its social evolution. This new viewpoint is founded on the results of nutritional surveys and clinical studies made in various regions of the country.

The first survey to ascertain the nutritional condition of our people was carried out under our supervision in the Northeast Zone of the country, in Recife, in 1932. This study covered 2500 people of the laboring class, and revealed that although these people spend an average of 71 per cent of their monthly salary on food, their habitual diet was inadequate in all respects except calories. This condition resulted from the low consumption of protective foods, i.e., meat, milk, eggs, vegetables, and fruit, their main diet consisting of beans, manioc flour, bread, coffee, and sugar. This survey was followed by three others in 1935, in the city of São Paulo in the south of the country. In this coffee producing and industrial zone, a superior economic region, no quantitative deficiency in nutrition was found, but the qualitative deficiency found in the Northeast region, also prevailed here. Nutritional surveys were made by the National Public Health Department during the years 1938 and 1939 in Rio de Janeiro and included 60,000 people. Diet in this zone was found to be high in calories, normal as to proteins, but deficient in minerals and vitamins. Other studies have been carried out in urban and rural zones of the country, on a smaller scale, and all revealed diets inadequate in one way or another.

This short paper does not permit us to give a complete impression of the various types of nutrition in a country the size of Brazil, with its 40,000,000 inhabitants spread over an area of 8,500,000 square kilometers. The area comprises a most varied range of climate and vegetation, from the equatorial forests of the Amazonian region to the temperate "pampas" of the extreme south. Its economic structure is varied, ranging from the simple rubber industry of the Amazon valley to the intensive coffee plantations and widespread industrialization of the State of São Paulo. In order to give at least a general idea of conditions a table is presented covering the five zones in which the country may be divided for purposes of nutritional study.

In all the zones, but principally in the first two, nutrition has always been inadequate because of these two factors: those of an economic nature, because a relatively low standard of living does not afford the laboring classes purchasing power for better nutrition, and those of a cultural nature arising from the ignorance of the people.

This inadequate diet is reflected in the physical state of our people. Although typical cases of classic avitaminosis arise only in limited zones and in certain periods, mild cases of hypovitaminosis and partial deficiencies of protein and minerals exist, widely spread throughout the entire territory. A hypochromic microcytic anemia, previously attributable to hookworm (Ankylostoma) infection, but in reality of

Zones	Geographical Structure	Basic Foods
I. Northern	This includes the great Amazon basin with its hot and humid climate, covered with equatorial forests.	Manioc flour, beans, fish, and crustaceans.
II. Northeast Coastal	The climate here is semi-humid. Sugar cane is the chief crop.	Manioc flour, beans, sweet potatoes, sweet manioc, and salt meat.
III. Central Zone of the Northeast	This region is semi-arid, covered with savannas and scrub forests. Goat raising is the principal industry.	Maize, beans, goat meat, cheese, and molasses.
IV. Middle West	This includes a central mountainous region as well as the low valleys of the Parana and Paraguay Rivers. Cattle and pigs are raised here.	Meat, beans, maize, bacon, and potatoes.
V. Southern	This region includes the plateau of São Paulo and the "pampas" of Rio Grande do Sul. The climate is temperate, and industry and agriculture flourish.	Meat, bread, rice, vegetables, and fruits.

nutritional origin due to iron deficiency, is endemic in Zones II and IV. Geophagia is common among children in these zones, which is explainable by specific iron deficiency.

In the Middle West Zone there is an iodine deficiency, which causes an alarming number of cases of thyroid hyperplasia.

In the Northern Zone the abundant and continuous perspiration caused by the climate, associated with the Indian habit of eating little salt, leads to a relative deficiency of sodium chloride, bringing about a chronic chloropenia which is apparent in the form of permanent fatigue.

Avitaminosis A in the form of xerophthalmia and hemeralopia, which in earlier times was widespread in the Northeast Zone, is today exceptional. The deficiencies in vitamin A are chiefly reflected in skin disorders and possibly in a reduction in resistance to infections.

The mild cases of hypovitaminosis of the B-vitamins constitute a more general deficiency condition. Beriberi epidemics, which took a heavy toll of lives in the State of Amazonas during the rubber development (1900 to 1913), have been completely overcome. Rickets is exceptional in Brazil because of adequate exposure to the sun. Cases of mild scurvy are frequently encountered in children. There is no pellagra zone in the country, this disease being a clinical rarity.

It is evident that the nutrition of the Brazilian people presents serious deficiencies and needs to be improved. Government authorities, influenced by scientists, have recently studied this problem, carrying out a series of measures following a systematic planning of a real national nutrition policy. Of these the following are of special significance:

(1) The minimum salary law introduced in 1937. This increased the purchasing power of the laboring classes and made it economically possible for them to improve their nutrition.

(2) The educational campaign. This has been instituted within the last few years, through the National Public Health Department, with a view to acquainting the people with the scientific fundamentals of good nutrition.

(3) The establishment in 1939 of the National Service of Food Assistance. This service aims to improve the nutrition of laborers by means of popular restaurants with low priced complete meals.

(4) The setting up of the National Food Bureau. This agency, established on the entry of Brazil into the war, is charged with the coordination, control, and orientation of all activities pertaining to the country's nutrition. As one of the sections of the Economic Mobilization, this new department has sought to organize, plan, and amplify our nutrition resources, with a view to ensuring the supply of food in the prevailing war emergency. The measures adopted in the various departments toward improving our nutritional conditions are far from

attaining their ultimate aim. This is explainable if we consider the complexity of the problem and the length of time the matter has been left without attention by the country's authorities. This subject is closely merged with the social and economic structure of the nation and cannot be tackled by itself nor uprooted from the social realities of which it is a natural consequence. Although the problem is not solved, Brazil is making good progress toward provision for good nutrition.

JOSUÉ DE CASTRO,
Chairman of the National Technical Nutrition Bureau, Professor of the University of Brazil, and President of the Brazilian Food Society.

DIETARY DEFICIENCIES AND THE GASTROINTESTINAL TRACT

Adequate nourishment depends not only upon the quality of the food ingested but also upon the efficiency with which the essential nutrients of the food are absorbed and utilized. Knowledge concerning the identity of dietary essentials, their distribution, stability, and requirements under normal circumstances has naturally developed more rapidly than knowledge of the physiologic and pathologic factors which influence their absorption and utilization. Although the possibilities have been recognized for some time and there is some evidence available on this subject, the importance of these conditioning factors as contributory causes of the deficiency diseases has not been generally recognized. There is great need for more careful observations and research in this field.

Jolliffe (*J. Am. Med. Assn.* **122,** *299 (1943)*) has reviewed and given references to many conditions which may influence gastrointestinal absorption. In addition to various gastrointestinal and biliary disorders, surgical resections, achlorhydria, continuous therapy with cathartics, colloidal adsorbents, and petrolatum, the effect of vitamin deficiencies themselves were included.

If the deficiency diseases can lead to an impaired intestinal absorption, which in turn aggravates the cause of the impairment by a further decrease in absorption, a vicious cycle may develop. The possibility also exists that the cycle once started, for example, by an outside cause, could continue long after the disappearance of the initiating agent and thus lead to confusion regarding etiology. There is much evidence to indicate that this may in fact be the case in sprue, celiac disease, and certain other diseases.

Studies on the influence of deficiency diseases on the gastrointestinal tract have been somewhat handicapped by the lack of a satisfactory experimental animal for this type of work. The gastrointestinal tract of the rat, guinea pig, dog, and chicken, those animals most amenable to dietary studies, differs greatly from that of man. Rao has published the results of studies of the "Intestinal Changes in Monkeys Fed on Poor Rice Diets" (*Indian J. Med. Res.* **30,** *273 (1942)*) which are of interest. One group of young monkeys (B) was placed on a diet similar to that regularly consumed by the poor sections of the population of southern India (rice eaters). Another group (A) received a diet representative of that regularly eaten by certain races in northern India. Diet B was composed primarily of rice but contained small quantities of vegetables, and pulses, while diet A included wheat, milk, vegetables, and butter in liberal quantities. The rice diet is poor, although not entirely free of vitamins A, C, the B-complex, and calcium.

The condition of animals in group A continued generally satisfactory. They gained weight, remained playful, and on autopsy showed only slight inflammatory changes of

the large intestine which were found to be due to occasional bacillary dysentery difficult to avoid in that part of the world. The monkeys on the poor rice eaters' diet soon failed to gain, became listless, and developed a chronic diarrhea. Early in the experiment this diarrhea could be stopped by additions of small amounts of protective foods. However, in the later stages of the disease the supplements were without effect in checking the diarrhea and the animals eventually died.

In addition to the gastrointestinal disorders, some animals in group B showed other signs of deficiency diseases. These included catarrhal ophthalmia, xerosis of the conjunctiva, lacrimation, swelling of the eyelids, pyorrhea, spongy and bleeding gums, wristdrop, and mild paralysis. The hair became coarse and sparse and the skin rough and scaly. Chronic indolent ulcers were frequently present. A few animals showed edema of the face, hands, feet, and scrotum, which responded to supplements.

The most important histologic change was a severe noninflammatory degeneration of the small intestine, lesions not shared by the large intestine. The jejunum and ileum were edematous and lined by a thick layer of mucus, and showed varying degrees of atrophy, being more marked in the lower ileum. The muscular layer was likewise atrophic. In cases surviving for longer periods, the villi were almost acellular, with the covering epithelium lost. This appearance is similar to the "withering villi" described by Mackie and Fairley (*Indian J. Med. Res.* **16,** *799* (*1929*)) in sprue. The protoplasm of the affected glands was granular and the nuclei were swollen. Although the muscular coat was atrophic, no other changes of the cells were noted and the serosa was normal. At no stage was inflammatory change observed.

McKenzie (*East African Med. J.* **17,** *30* (*1940*)) described a clinical condition occurring in African laborers subsisting on poor diets which appears to be identical with that observed in the monkeys. The name "nutritional diarrhea" was given to this condition. The gastrointestinal symptoms and the histologic appearance of the gut in these cases were essentially similar to those in the monkeys. Likewise it seems probable that the high incidence of diarrhea of unknown etiology seen among the poorly nourished in other parts of the world might have the same origin.

McCarrison, a number of years ago ("Studies in Deficiency Diseases," *Oxford Medical Publications, London* (*1921*)), carried out experiments which likewise emphasized the possibility of the vulnerability of the gastrointestinal tract to dietary deficiencies. Numerous papers on sprue, celiac disease, pellagra, and tropical diarrheas implicating the deficiencies have appeared in the meantime. As mentioned before, the lack of a satisfactory experimental animal has delayed studies on the relation of the deficiency diseases to the gastrointestinal tract. Increased use of the monkey for this type of investigation would seem wise. Experiments involving milder degrees of deficiency with both physiologic and pathologic observations are needed.

AVAILABILITY OF CALCIUM AND PHOSPHORUS IN CHOCOLATE MILK

Many nutritionists who have endorsed the inclusion of cocoa in milk as a means of adding more widespread appeal to this protective food will be interested in recent data which cast some doubt on the soundness of this practice through long intervals of time. That many diets are low in available calcium is generally recognized. Research work at Massachusetts State College by Mueller and Cooney (*J. Dairy Sci.* **26,** *951* (*1943*)) indicates that these diets may be rendered even more deficient if cocoa is used excessively as an added flavoring constituent.

Earlier work by Lipman and Mueller (*J.*

Dairy Sci. **24,** *399 (1941)*) indicated that cocoa decreased the digestibility of milk proteins. To this observation, Mueller and Cooney now add the results of a study on the possible interference with proper utilization of calcium and phosphorus in the milk when cocoa is present.

Using albino rats (age, 25 days), the authors selected litter mates into groups of three having similar weights and sex. One of each of the twelve groups of males and nine groups of females was fed a control diet consisting of 52.9 g. of whole milk powder and 31.1 g. of sucrose. Iron, copper, and manganese salts were fed daily as a mineral supplement. The second animal in each group received a similar diet to which was added 16.0 g. of cocoa powder, but feeding of these paired animals was restricted so that the rats receiving the cocoa supplemented diet consumed the same amounts of the basal ration ingredients as did the control animals. Accordingly, the extra food intake of the one group was entirely in the form of cocoa which accounted for 16 per cent of the solids in the test diet. The third rat in each of the twenty-one groups was sacrificed at the start of the feeding period in order to obtain the calcium and phosphorus contents of the carcass from which to calculate the retention of these minerals in the rats on the two diets. After a five week feeding period during which the animals were weighed weekly, the test animals were killed and a final weight obtained after removal of the contents of the gastrointestinal tract. The amounts of calcium and phosphorus in the carcass were then determined.

The data reported by Mueller and Cooney indicate that the presence of cocoa resulted in depression of the nutritional value of the milk whether measured in terms of growth, calcium utilization, or phosphorus retention. Despite the fact that the animals on the cocoa supplemented diet received 11 per cent more calories than the control group, there was a 10.6 per cent average decrease in growth rate for the males, a 12.3 per cent decrease for the female rats that could be attributed only to the fact that cocoa was present in the diet. As a partial explanation for this depression in the growth rate, the authors cite the lowered availability of the protein and the growth retarding effect of the substances in cocoa.

The data on calcium retention are even more striking. The rats on the cocoa diet retained 24.8 and 22.0 per cent less calcium than the controls (males and females, respectively), despite a somewhat higher calcium intake on the former diet. That the decreased retention of calcium is not due to the lowered growth rate is evident from the data calculated on a 100 g. body weight basis. Figures on this basis showed a depressed calcium utilization of 18.0 and 15.3 per cent for the two sexes and are, according to the authors, statistically significant.

Although the cocoa contained an appreciable amount of oxalic acid (0.54 per cent), the reduction in calcium retention could not be attributed to the formation of unabsorbed calcium oxalate. The oxalic acid could bind a maximum of 7.8 per cent of the calcium in the cocoa supplemented diet, whereas the observed decrease in calcium retention was three times this amount.

Male and female rats on the cocoa diet showed decreases in phosphorus utilization of 22.1 and 17.8 per cent, respectively. On an equal weight basis, these groups of animals show a depressed retention of phosphorus of 15.2 per cent for males, 10.7 for females. When analyzed statistically by the method of Student, these differences also proved to be highly significant. The reduction in the amount of phosphorus utilized by rats receiving cocoa in addition to the basal milk diet is particularly striking, since these animals were receiving 30 per cent more phosphorus than the controls because of the large contribution of this mineral from the cocoa.

The underlying cause or causes for the decreases in growth rate and mineral retention when rats are placed on a diet of chocolate milk cannot be adequately explained on

the basis of data presented. The implications of the results are, however, apparent. With a sharp curtailment in milk supplies becoming imminent, the need for maximal utilization of the protein and mineral nutrients of milk becomes increasingly important. Comparable studies in human nutrition apparently have not been conducted.

PASTURE FEEDING AND VITAMIN A IN COW'S MILK

In 1913 Casimir Funk (*Biochem. J.* **7,** *211 (1913)*) made one of his many accurate generalizations in which he predicted that it would be found that a definite relationship exists between the vitamin secreted in milk and that ingested in the food. At that time vitamin B was thought to be a single entity, vitamin A was yet to receive its alphabetical designation, and vitamin C was not yet recognized.

Similar conclusions were voiced by McCollum, Simmonds, and Pitz (*J. Biol. Chem.* **27,** *33 (1916)*) three years later, basing their statements on the deportment of young nursing rats. It was, of course, impossible at that time to measure the vitamin content of rats' milk. Similarly, Steenbock, Boutwell, and Kent (*J. Biol. Chem.* **35,** *517 (1918)*) observed that butterfats varied in vitamin A potency and suggested that the vitamin A content of the ration might have been responsible for these variations. Similar explanations regarding the variability in the vitamin A content of milk were advanced by Hess, Unger, and Supplee (*J. Biol. Chem.* **45,** *229 (1920–21)*). In 1922 Kennedy and Dutcher (*J. Biol. Chem.* **50,** 339 (1922)) described experiments in which milk from cows, on "vitamin-poor" and "vitamin-rich" rations, was fed to rats as a source of vitamin A. It was concluded that the vitamin A potency of the experimental milks was definitely related to the vitamin A content of the ration.

In subsequent years many laboratories confirmed these observations and have shown that the vitamin A potency of milk and butter depend upon the carotene content of the ration, this pigment being deposited in the milk fat partly as carotene, *per se*, and partly as vitamin A. The nonpigmented breeds, such as the Holstein, seem to be able to convert larger proportions of the ingested carotene to vitamin A and, consequently, excrete more vitamin A and less carotene in their milk than is the case with the so-called pigmented breeds such as the Jersey and Guernsey. The latter breeds might be said to exist in a partial state of carotenemia, due to their characteristic inability to transform carotene efficiently into vitamin A.

A few laboratories have turned their attention to the vitamin A requirement of the bovine with the view of establishing the minimum requirement for (a) growth, and (b) growth, reproduction, and milk production. For example, Guilbert, Miller, and Hughes (*J. Nutrition* **13,** *543 (1937)*) concluded, as a result of feeding experiments on cattle, sheep, and swine that these species require about 25 micrograms of carotene per kilogram of body weight. This figure, they believe, is the absolute physiologic minimum requirement. The practical minimum is probably five to ten times this amount. Converse and Meigs (*J. Dairy Sci.* **21,** *Supplement 114 (1938)*) state that cows require about 80 to 100 mg. of carotene per day during the last months of gestation to ensure normal healthy calves.

It is generally agreed that summer butters are richer in vitamin A and carotene than winter butters, owing to the higher content of carotene in fresh pasture grasses. Hauge (*Food Industries* **14,** *48 (1942)*) states that if cows are expected to produce a butterfat of maximum vitamin A potency they should receive a daily intake of 550,000 units of vitamin A when alfalfa is the

source of carotene. Most workers have found it difficult, if not impossible, to produce milk or butter with winter rations which can compare in vitamin A potency with that produced on good pasture in the summer. Of course it is possible to produce winter milk of high vitamin potency by feeding shark liver oil or grass and legume silage.

Studies along these lines have been made by Koehn (*J. Dairy Sci.* **26,** *673 (1943)*). This investigator, stationed in Alabama, felt that climatic conditions in the South favor long grazing periods and the production of winter pastures. It was felt, therefore, that it might be possible for southern dairymen to produce winter milk which would compare favorably in vitamin A content with summer milk. The experiments were planned to obtain data on (1) normal seasonal fluctuations in the vitamin A content of milk, (2) the value of commonly used roughages as a source of carotene during the winter months, and (3) the effect of temporary winter pastures on the vitamin A potency of milk.

Carotene and vitamin A were determined by a method developed by the author, using a photoelectric colorimeter (Koehn and Sherman, *J. Biol. Chem.* **132,** *527 (1940)*). Crystalline vitamin A alcohol was used in establishing a calibration curve and results were recorded in terms of micrograms of vitamin A. Carotene in forage was determined by the method of Peterson, Hughes, and Freeman (*Ind. Eng. Chem. (Anal. Ed.)* **9,** *71 (1937)*).

In experiments which lasted for sixteen months it was found that cows which were permitted access to permanent pasture throughout the year produced milk which varied from a minimum of 200 micrograms per quart of vitamin A to a maximum of 1045 micrograms per quart. Starting in October the milk assayed 535 micrograms per quart. This decreased steadily during November, December, and January until the minimum of 200 micrograms per quart was reached in February. From that point the vitamin A potency of the milk increased steadily until the maximum of 1045 micrograms per quart was reached in the following August. The potency then decreased rather rapidly until, in the following January, the vitamin A activity of the milk had fallen to a winter level of around 290 micrograms of vitamin A per quart. In explanation, it should be stated that the method of the author expresses the vitamin A activity as the sum of the vitamin A and carotene values. In calculating the total micrograms—vitamin A equivalents—he assumes that 2 micrograms of carotene are equivalent to 1 microgram of vitamin A.

The experiments were so arranged that temporary winter pasture consisting of rye and clover became available for use in February when normal herd milk was lowest in vitamin A content. When cows were placed on the special winter pasture the vitamin A potency of the milk increased fourfold, reaching 800 micrograms per quart before the end of February and a maximum in May when the vitamin A potency of the milk exceeded, by a small amount, that obtained in the maximum month (August) on summer pasture.

A study of the effect of different roughages on the vitamin A potency of winter milk showed that sorghum silage, permanent pasture, and a poor grade of alfalfa hay had little effect. Peanut and Lespedeza hays of good quality caused a slight increase in the vitamin A content of milk, while the feeding of carotene rich Puerto Rico sweet potatoes increased the vitamin A potency about 40 per cent. A good growth of temporary rye pasture was superior to a temporary pasture consisting of oats which had been stunted due to cold weather. Analyses showed, as was expected, that the carotene content of temporary pasture forage was considerably higher than that of the permanent pasture.

It is unfortunate that the vitamin A potency of milk and butter reaches a mini-

mum value during the winter months, for this is the time of year when other vitamin A rich foods of the human dietary are also low. However, extensive experiments in this country and abroad have shown that the potency of winter milk can be increased 50 per cent or more by the use of grass and legume silages. Such silages are not in general use since methods of preserving them have been perfected only within the last few years and new agricultural practices are adopted slowly. Moreover, dairy farmers receive no premium at the present time for a product of greater nutritional value.

Koehn pointed out that only during four months of the year was it possible to produce milk of such vitamin A potency that 1 quart would furnish one-half the recommended daily allowance (5000 I.U. or 1500 micrograms). In midwinter 1 quart furnished about one seventh of the daily allowance. It is of interest to compare these figures with those obtained by Dornbush, Peterson, and Olson (*J. Am. Med. Assn.* **114,** *1748 (1940)*), who assayed a large number of market milks in Wisconsin. These authors also observed a rapid decrease in vitamin A potency during November and continuing to April. In this northern state the rise in potency comes somewhat later than in the South, in April rather than March. It is of interest that the lowest average values obtained in the winter and spring in Wisconsin were somewhat higher than those reported by Koehn in Alabama. It thus appears that good succulent feed is necessary to maintain the vitamin A and carotene content of the milk at a high level, and permanent pasture may have relatively little advantage in this respect over the feeding practices generally used in the northern states. On the other hand, temporary pasture provides a practical method for the southern farmer to improve the nutritive value of winter milk.

THE USE OF SODA IN THE COOKING OF PEAS

Sodium bicarbonate is often employed in the cooking of green vegetables since, by its use, the cooking time may be considerably shortened and the desirable green color appears to be enhanced. The possibility that the addition of soda may so alter the pH that destruction of vitamins may be increased has led many nutritionists to feel that its use should be discouraged. Much of the reasoning behind this is purely theoretical, and adequate data on the destructive effect of sodium bicarbonate in the cooking water have not been available. Accordingly, a recent paper by Johnston, Schauer, Rapaport, and Deuel (*J. Nutrition* **26,** *227 (1943)*) is of timely interest.

These workers studied the effect of cooking with and without sodium bicarbonate on the thiamin, riboflavin, and ascorbic acid content of fresh and of frozen peas. For the purposes of their experiment, 85 g. of peas were cooked with 180 ml. of water, and when sodium bicarbonate was used, 0.22 g. was added. This quantity of bicarbonate equals or exceeds that recommended by home economists sanctioning the use of this material. Preliminary tests showed that bicarbonate reduced the required cooking time, as judged by tenderness of the peas, from seventeen to eight minutes for fresh peas, and from six to four minutes for the frozen peas. These cooking times were used throughout the study. The peas were added to the boiling water and after cooking, were filtered from the cooking water, homogenized in a Waring Blendor, and the macerated tissues and cooking water were examined for the vitamin content. Thiamin was determined by the yeast fermentation method of Schultz, Atkin, and Frey (*Ind. Eng. Chem.*

(*Anal. Ed.*) **14,** *35* (*1942*)). The applicability of this method of analysis was confirmed by bioassays. Riboflavin was determined microbiologically by the method of Snell and Strong (*Ind. Eng. Chem.* (*Anal. Ed.*) **11,** *346* (*1939*)), while ascorbic acid was determined by the colorimetric method of Loeffler and Ponting (*Ibid.* **14,** *846* (*1942*)).

The effect of addition of sodium bicarbonate was to raise the pH of the cooking water from approximately 7.5 to 8.7 to 8.8. For fresh peas and for peas frozen by the tunnel-freezing process, no loss of thiamin was obtained during cooking with tap water, although 20 per cent of the thiamin leached into the cooking water. Essentially no loss was obtained when the peas had been prepared by plate-freezing, but here approximately 32 per cent of the thiamin appeared in the cooking water. The greater amount of leaching is ascribed to the partial rupturing of the cell membranes of the peas frozen by this process. When the same products were cooked in the presence of sodium bicarbonate, the fresh and the tunnel-frozen peas showed negligible losses of thiamin, and leaching into the cooking water was identical with that found when tap water alone was used for cooking. The peas that had been frozen by the plate-process, however, lost 38 per cent of the total thiamin, most of the loss being attributed to a destruction of the vitamin in the more alkaline cooking water. When fresh peas were overcooked, large thiamin losses were obtained, 60 per cent when soda was used, and 45 per cent in water alone.

With riboflavin, a maximum of 14 per cent of the vitamin was lost in the cooking process, the frozen product showing slightly greater losses than for fresh peas. The presence or absence of soda in the cooking had no demonstrable effect on the leaching or destruction of riboflavin from fresh or frozen peas. Retention of the vitamin in the peas varied from 64 to 70 per cent.

The presence of sodium bicarbonate produced no effect on the retention of ascorbic acid during the cooking of several types of frozen peas or of fresh peas. Considerably more destruction was observed for frozen peas than for fresh peas, 15 to 20 per cent being lost in the former as against a maximum of 8 per cent for the fresh material. Again, the peas frozen by the plate-process showed a much higher diffusion of the vitamin into the cooking water than peas prepared by tunnel-freezing. Retention in the latter was approximately 60 per cent; only 45 per cent of the total ascorbic acid remained in peas frozen by the plate-process.

This study indicates that with proper allowance for a shortened cooking time, the use of small amounts of sodium bicarbonate in the cooking of peas will not affect the riboflavin or ascorbic acid content of the product as prepared for the table. The data for thiamin, however, indicate the need for caution in sanctioning the use of soda during the cooking of vegetables. The evidence points to a considerable destruction of this vitamin that can be ascribed to the soda if the vegetable has been processed or handled in a manner likely to cause rupture of the membranes (e.g., certain brands of frozen peas).

As the authors noted, the buffer effect of the constituents in peas is considerable, probably much more than for other vegetables. It is to be hoped that other vegetables will be studied in cooking tests such as this in order that the advantages or disadvantages in the use of soda can be truly evaluated. A major objection to the use of soda has been that the housewife does not add accurately measured amounts of sodium bicarbonate, and may have excessive amounts of this alkali in the cooking water. Minimal cooking times are not always used, particularly when the vegetable is not totally consumed and is saved for another meal. The data reported in the paper by Johnston and co-workers, if anything, emphasize the undesirability of the addition of soda under such conditions.

MAXIMUM LIMITS OF NITROGEN ASSIMILATION

It has been found possible to maintain normal nitrogen balance or even to correct protein deficiencies by intravenous administration of amino acids or casein hydrolysate (*Nutrition Reviews* **1,** *284, 345, 379 (1943)*); Martin and Thompson, *Medicine* **22,** *73 (1943)*). There has been little information, however, as to the rate at which these materials can be utilized when injected. Elman, Charnas, and Davey (*Arch. Surg.* **47,** *216 (1943)*) have provided some experimental evidence on this point. They produced protein deficiency and hypoalbuminemia in dogs by feeding a mixture of corn syrup, Ringer's solution, and a vitamin B-complex concentrate for a three week period. Continuous intravenous injection of a casein hydrolysate was carried out with the animals suspended in a Pavlov frame. Determinations were made of the fractional serum proteins, plasma volume, hematocrit, and urinary excretion of both total and amino acid nitrogen.

In the first experiment enough of the hydrolyzed protein (10 per cent solution) was injected in a twenty-four hour period to provide 3.5 g. of nitrogen per kilogram of body weight. There occurred only a transient increase in serum albumin, caused by hemoconcentration. Almost all of the parenterally administered nitrogen was excreted during the following week, and the serum albumin level actually fell lower than it had been before the therapy. In one dog, nearly 25 per cent of the administered amino acids was excreted in the urine on the day of venoclysis. Addition of 5 per cent glucose to the hydrolysate did not result in any better utilization of the nitrogen. Amazingly large amounts of fluid (280 to 560 ml. per kilogram of body weight) were given in the injections, but the authors claim that these were well tolerated, other than causing an occasional transient edema of the injected leg.

Utilization appeared to be much better when a similar amount of the hydrolyzed protein was injected over a forty-eight hour period. The solution for these experiments contained 7.5 per cent of the hydrolysate and 2.5 per cent glucose; 1.75 g. of nitrogen per kilogram per dog was provided, an amount which corresponds to 11 g. of protein per kilogram. A sustained increase in both serum albumin and globulin occurred and there was no extra excretion of nitrogen during the week after therapy. In the 2 dogs used, the albumin increase in the whole circulating blood volume was 2.9 and 3.4 g.; the total nitrogen retained was approximately 26 g., or (x 6.25) over 160 g. of protein. The serum protein regeneration, therefore, accounted for only a fraction of the retained nitrogen and a large increase in tissue protein was assumed.

The 2 dogs used in these studies had the ability to utilize at least 1.75 g. of nitrogen (11 g. of protein) per kilogram every twenty-four hours for two days. How long they would have been able to continue at this pace was not determined. The study suffers from the fact that all of these studies were done on only 2 animals. It is furthermore difficult to understand why if one rate of injection produces a rather marked retention, double this rate allows of practically no retention.

There are no comparable studies on human subjects to indicate the maximum amounts of protein which may be assimilated. Brunschwig, Clark, and Corbin (*Ann. Surg.* **115,** *1091 (1942)*) gave 150 g. of a casein hydrolysate intravenously for ten consecutive days to a patient weighing 50 kg., and twice this amount was given daily for three days to 2 patients without difficulty (Elman, Weiner, and Bradley, *Ann. Surg.* **115,** *1160 (1942)*). Hartmann, Meeker, Perley, and McGinnis (*J. Pediatrics* **20,** *308 (1942)*) showed that growing children given protein both as food and as a casein

hydrolysate were able to assimilate as much as 10 g. of protein per kilogram per day. Although there are comparatively few clinical circumstances in which it is either necessary or desirable to strain the ability of patients to utilize nitrogen, it is nevertheless desirable to establish the tolerable limits of amino acid assimilation.

THE NUTRITIVE VALUE OF KERATINS

Keratins have always been characterized by insolubility and resistance to digestion by common proteolytic enzymes. It is, therefore, somewhat startling to learn from reports in the literature that wool, feathers, and swine hoofs, when finely powdered, have been found to have some nutritive value as sources of protein.

Routh and Lewis (*J. Biol. Chem.* **124,** *725 (1938)*), in studying tryptic digestion of wool, increased the state of subdivision of the wool fibers by prolonged grinding in a ball mill, and produced powdered wool which was readily digested by trypsin and pepsin. Routh (*J. Biol. Chem.* **135,** *175 (1940)*) suggested that grinding in a ball mill produces a degradation of wool protein accompanied by oxidative changes and an appreciable decrease of cystine in the powdered material.

These observations suggested the possible utilization of powdered wool by animals. Consequently, Routh continued his studies with the view of determining if finely powdered wool could be utilized by rats as a source of protein (*J. Nutrition* **23,** *125 (1942)*). The powdered wool was prepared by grinding for 500,000 revolutions in a ball mill. Preliminary studies indicated that powdered wool, as the sole source of protein in an otherwise adequate diet, was incapable of supporting growth in young rats. However, animals thus fed lived longer and lost weight less rapidly than controls on a nitrogen free diet. Diets containing 15 and 20 per cent of powdered wool were fed to rats. It was found that tryptophane, methionine, histidine, and lysine were present in suboptimal concentration in the powdered wool, but that moderate growth of rats could be obtained if the basal diet was supplemented with these amino acids.

Routh extended these investigations to include a study of the nutritional value of powdered chicken feathers (*J. Nutrition* **24,** *399 (1942)*). The feathers used in this feeding experiment were ground for 400,000 revolutions in a ball mill, since *in vitro* digestion tests with trypsin had been found to reach a maximum with feathers which were ground for this period. The ground feathers constituted 15 per cent of a diet which was otherwise adequate except for protein, and were compared with powdered wool and casein as sources of protein.

As was true in the case of wool, tryptophane, methionine, histidine, and lysine were found to be lacking in optimum concentrations in feathers, but moderate growth resulted when these amino acids were added to the diet containing feathers. The data suggest that feathers contain less lysine than wool. When 5 or 8 per cent of casein was used as the supplement instead of the above amino acids, the growth rate was essentially the same, but rats grew only one-fourth as rapidly when 3 per cent of casein was used. Powdered wool supplemented with 3 per cent of casein produced a definitely higher growth rate than the same diet containing feathers.

Further work has been reported recently by Wagner and Elvehjem (*Poultry Sci.* **22,** *275 (1943)*) who have investigated the nutritive value of powdered swine hoofs. Previous unpublished work by Wagner and Elvehjem demonstrated that digestibility *in vivo* was greatly increased when swine hoofs were ground to a fine powder. The

powdered hoofs were used readily as a source of protein by rats and chicks and were found to be more adequate for the nutrition of chicks than purified casein.

In a later experiment conducted with White Leghorn chicks, these workers fed powdered hoofs in combination with a low protein basal ration composed of practical poultry feed ingredients plus skim milk powder. A series of rations were fed to test the supplementary growth effects of powdered hoofs, meat scraps, fish meal, and expeller-type soybean meal. Judging by growth response, the results indicated that the powdered hoofs are a satisfactory substitute for meat scraps and fish meal in a practical poultry ration. The authors suggest that because of their amino acid makeup, keratin proteins may be of particular value for animals which produce quantities of keratin containing tissue, such as feathers.

Alteration of the characteristic properties of proteins by grinding is not new, having been previously demonstrated with gelatin by Alsberg and Griffing (*Proc. Soc. Exp. Biol. Med.* **23,** *142 (1925)*) and by Boissevain (*Am. Rev. Tuberc.* **31,** *542 (1935)*). The nature of all changes involved is not completely known, but chemical as well as physical changes are thought to occur. Increase in surface area attending the reduction in particle size, achieved through grinding, may partially account for the ability of enzymes to digest keratins. However, analyses of wool fractions of varying particle size have been shown to be uniform, while marked changes in the composition of wool have been produced in samples which have been ground for varying periods. Thus, it is thought that oxidative changes accompany the mechanical degradation of the protein. The net result, in powdered wool, is the production of a water soluble fraction containing nitrogen and sulfur, with an attendant loss of cystine from the wool. Increased amounts of nitrogen, cystine, inorganic sulfates, and the intermediate oxidation products of cystine are found in the aqueous extracts.

While further research along this line would be highly desirable, it is apparent that the basic changes, either physical or chemical, which are brought about in keratins by reducing them to an extreme state of subdivision, produce a material which has definite nutritive value. Economically from the viewpoint of the nutrition of livestock, keratins have always been regarded as waste products. Now it appears that these protein rich materials may find new usefulness as components of practical feeds, especially under conditions of wartime protein shortage.

NUTRITIONAL SURVEY OF A RURAL POPULATION IN TENNESSEE

The assessment of the nutritional status of an individual, or a group of individuals, necessitates not only an accurate dietary history but in addition a reasonably complete physical and laboratory examination. It is only from the accumulation of this information that it will be possible to evaluate the validity of certain implied and suggested relationships between clinical and laboratory findings and the patient's dietary history. The difficulties which stand in the way of carrying out such a program are well known, yet sound conclusions will be possible only from careful studies of this type. The use of large groups of subjects would seem desirable since such information as is obtained can be subjected to statistical analysis for determining significant correlations. On the other hand, with the use of large groups it is not always possible to obtain maximum accuracy in the dietary histories, physical examinations, and laboratory studies. It remains a question as to whether a small group thoroughly and repeatedly studied will

yield more reliable information than a large group less thoroughly investigated.

Youmans *et al.* (*Am. J. Pub. Health* **32,** *1371 (1942);* **33,** *58, 955 (1943)*) carried out a complete survey of a predominantly rural area of middle Tennessee. The survey included a record and study of food consumption on both a household and individual basis, a medical history, physical examination, and various laboratory tests. A seven day record was obtained for household consumption, and a three day record for individual consumption. Considerable care was taken to insure the accuracy of the data. The dietary intakes were calculated from standard tables of food values, making some adjustments for season of the year, vitamin losses due to cooking, etc. All histories and physical examinations were done by physicians with some training in nutrition. Children under 4 years of age were examined by pediatricians. A total of some 1200 individuals was studied, one-third being Negroes. The age groups ranged from less than 3 months to 99 years of age, about 50 per cent falling between 21 and 60 years.

In the first report (*Nutrition Reviews* **1,** *302 (1943)*) the relation of caloric intake to history of obesity or underweight and the state of subcutaneous tissue and musculature in relation to height and weight was studied. Over 90 per cent of the subjects had their first examination in the late summer and fall, the remainder in the late winter and spring. With the exception of the 1 to 6 year old white group, the mean caloric intakes of the different age groups were found to be significantly less than the daily allowances recommended by the Food and Nutrition Board of the National Research Council (*Nutrition Reviews* **1,** *164 (1943)*). This deficit was found to increase irregularly with increasing age and was greater in the Negroes. The deficit ranged from 274 calories in the 7 to 9 year old male and female whites to a maximum of 1735 calories in the 16 to 20 year old Negro males. On the basis of 1250 calories as a minimum intake for all ages over 1 year, 14.3 per cent of the white subjects and 42.1 per cent of the Negroes, or 23.4 per cent of all subjects 1 year old or older, had intakes below the recommended allowance. While the caloric intake indicated serious undernutrition in a large portion of this group, the weight records of the subjects did not support this prediction. Thus it was not possible to establish an unequivocal correlation between these two findings. Furthermore there was no x-ray evidence of a delay in growth and maturation of the skeletal system of the children.

The inconsistency of the findings would point to two possible errors. The first of these is that the calculated caloric intakes were inaccurate. The magnitude of the discrepancy, however, appears to be well outside the range of error particularly since this is one of the more reliable estimations in diet assessment. The second and more likely possibility is that the recommended daily allowances as set up by the Food and Nutrition Board of the National Research Council are too high. In this connection, it is of interest to note that in a survey of a North Carolina community representing about 400 people, Milam (*Am. J. Pub. Health* **32,** *406 (1942)*) found the average daily caloric intake to be only 2000.

In the study on the protein nutrition of this same population, the protein content of foods was calculated from standard reference tables. All the subjects were questioned concerning the occurrence of edema in the past, and all were examined for presence of same by the usual method of pitting on pressure. Serum proteins were determined in part by the macro-Kjeldahl method using Howe's procedure for separation of albumin, and in part by the biuret technic of Robinson and Hogden (*J. Biol. Chem.* **135,** *707* (1940)).

The majority of the subjects had a daily protein intake below that recommended by the Food and Nutrition Board of the National Research Council. Low intakes (below 50 g.) were more frequent in Negroes than in whites, 50 and 32 per cent respec-

tively. In white children under 13 years of age low intakes were found in from 4 to 12 per cent. In the age groups 13 to 15, 16 to 20, and greater than 21 years, it was found that 10, 13, and 9 per cent of the white males and 58, 24, and 44 per cent of the white females, respectively, showed low protein intakes. Corresponding values for the Negroes were 61 and 92 per cent in the children, 36, 24, and 27 per cent for the males, and 85, 62, and 69 per cent for the females, respectively. Similar deficiencies were found in respect to animal protein intake with the Negroes showing a low intake (less than 20 g.) more often than the whites (63.9 and 30.1 per cent, respectively).

A history of edema was obtained from 49 whites and 33 Negroes. Most of these subjects were adult females (75 per cent). Only 10 per cent of the white subjects and 18 per cent of the Negroes who gave a history of edema actually had edema on examination. Of the entire group only 3 per cent had serum protein levels below 6 g. per 100 ml. However, in 9 per cent of the whole group serum albumin was below 4 g. per 100 ml., representing 13.1 per cent of the Negroes and 6.9 per cent of the white subjects, respectively. Rather striking differences were observed between the various age and sex groups. Thus, serum albumin levels below 4 g. per 100 ml. were infrequent in white and Negro children below 13 years of age. The highest incidence was found in Negro females 16 to 20 years of age (29 per cent) and Negro women 21 and over (24 per cent). White females of the same age group showed 10 and 8 per cent, respectively.

The great deficiency of protein intake in this large group, when compared with the recommended allowances of the Food and Nutrition Board, is all the more striking when it is recognized that these individuals also had a great deficiency in caloric intake. A low protein, high caloric diet might be considered adequate to maintain an adult in nitrogen balance if the protein has high biologic value. However, in this group, not only were the caloric and protein intakes low, but in addition the animal protein intake was low. In spite of these apparently severe restrictions in protein intake, the incidence of low serum protein levels was not great, and failed to reflect as great a deficiency of protein as would appear probable from the dietary studies. Further, there was no demonstrable correlation between the serum albumin levels and the total intake of calories, protein, and animal protein. There was likewise no relationship between the history and presence of edema and the serum protein levels. In considering the possible explanation for the failure to find a correlation between protein intake and serum protein levels, the authors raise the question as to whether the estimation of the latter can be employed as a method for determining the former condition. While clinical and experimental evidence support the view that there is a relationship between the serum protein levels (particularly albumin) and protein intake, the dietary restrictions apparently must be more severe than those encountered in this study.

It is apparent from this large and well planned study that the correlations hoped for between dietary histories, physical examinations, and laboratory procedures in cases of marginal or even moderate dietary deficiencies are not well established. It further appears that the daily allowances recommended by the Food and Nutrition Board of the National Research Council may be set too high, at least for this population, as regards calories and proteins adequate for measurable health.

VITAMIN LOSSES DURING STORAGE OF DEHYDRATED VEGETABLES

The preservation of foodstuffs by dehydration both commercially and in the home has increased enormously during the past two years. Experiences with dehydrated

foods during the last war revealed a marked change in palatability, color, odor, and vitamin content after storage and shipping. Certain of these undesirable changes have been studied and to some extent prevented by proper treatment of the fresh foods. Thus precooking (blanching) of vegetables previous to dehydration has been shown to result in better retention of carotene and ascorbic acid on storage. However, detailed studies on losses of vitamins during dehydration and storage have been relatively few. Recently Tressler, Moyer, and Wheeler (*Am. J. Pub. Health* **33**, *975 (1943)*) have investigated the losses of carotene, thiamin, and ascorbic acid during the commercial dehydration of cabbage, beets, rutabagas, and potatoes, and further, the rate of loss of these vitamins during subsequent storage under various conditions. Storage conditions included packaging in glass containers, under carbon dioxide in glass containers, and in either moisture-proof cellophane or pliofilm bags. The storage temperatures ranged from −40° F. to 75° F.

Dehydration itself resulted in very little loss of carotene from any of the vegetables. However, at all storage temperatures above −40° F. there was a rapid loss. Storage under carbon dioxide reduced the loss of carotene, especially at the higher temperatures. Dehydration and storage were found to result in very little loss of thiamin, the greatest losses of this vitamin occurring during the blanching process previous to dehydration. Ascorbic acid losses were great with all the vegetables. Dehydrated potatoes contained only a trace of ascorbic acid, and beets lost about one third of their original ascorbic acid content after dehydration, but the original levels were very low (0.24 mg. per gram dry weight). Water blanching and dehydration resulted in an 85 per cent loss of ascorbic acid from rutabagas. At temperatures of 58° F. and above, more than half the remainder was lost after four months storage. At lower temperatures the losses on storage were smaller. Storage under carbon dioxide had little effect on the rate of loss of ascorbic acid. Cabbage, in contrast to the other vegetables, showed only a 20 per cent loss of ascorbic acid during dehydration and practically no loss during storage at −40° F. for three months. Analysis at this time showed the ascorbic acid content to be more than 3 mg. per gram of dehydrated cabbage.

It is apparent from this study that the vitamin losses from vegetables during preparation, dehydration, and subsequent storage are large, especially as regards ascorbic acid, and to some extent carotene. The continued increase in the use of dehydrated foods will necessitate a more careful inquiry into dietary histories where nutritional evaluation is desired.

CYSTINE AND TUMOR FORMATION

During the last few years investigators interested in the relation of diet to cancer have tended to place increasing emphasis on effects due to specific dietary substances such as vitamins and amino acids. One of these is cystine. This substance seems to be required by the animal for the optimal development of tumors produced by a wide range of carcinogenic factors. By way of contrast it has also been reported that under special experimental conditions the combination of cystine and choline tends to suppress the formation of liver tumors due to p-dimethylaminoazobenzene (György, Poling, and Goldblatt, *Proc. Soc. Exp. Biol. Med.* **47**, *41 (1941)*).

In all experiments with cystine the basal diets employed are fairly high in fat and low in total protein as well as in cystine. The diet used most extensively (White and Mider, *J. Nat. Cancer Inst.* **2**, *95 (1941–42)*), contains 25 per cent fat and only 3.9 per

cent casein. Surprisingly, young rats or mice placed upon this diet not only managed to survive for many months but they usually grew at a steady though suboptimal rate. The addition to the basal ration of a carcinogenic hydrocarbon or of an azo dye such as p-dimethylaminoazobenzene reduced this growth to a virtually negligible rate, but the further addition of 0.5 per cent cystine restored growth even in the presence of the carcinogen. The explanation offered was that cystine is needed to combine with the hydrocarbons or the azo dyes in the process of detoxification; and that on diets low in this amino acid the available cystine is entirely used up by the foreign molecules so that inadequate cystine is left to be combined into body protein. Addition of cystine to the diet enables new tissue to be manufactured and growth is resumed.

However, in spite of its role in detoxification, cystine has been found to promote the formation of experimental tumors due to carcinogenic chemicals. White and Mider painted strain dba mice for one hundred days with an ether solution of methyl cholanthrene and observed an incidence of leukemia in only 17 per cent of their animals fed the diet low in protein and in cystine. When an additional 0.5 per cent of cystine was incorporated into this diet, the incidence of leukemia rose to 95 per cent. Mice fed a commercial dog biscuit throughout the experiment likewise showed a high incidence of leukemia, 89 per cent. Obviously if the only effect of cystine were on detoxification, the effectiveness of the methyl cholanthrene should have been decreased rather than increased in the presence of the cystine. The effect actually observed, therefore, must have been related to some other mechanism —possibly to the better physical condition of the animals fed the amino acid.

In the absence of the hydrocarbon, dba mice fed the low cystine diet had rough coats, failed to grow, and did not breed. When 0.5 per cent of cystine was added to this diet the mice gained weight and the females bore average sized litters. Little difference could be noted between mice ingesting the cystine-supplemented diet or the commercial dog chow. Evidently, therefore, the low level of protein *per se* did not appreciably modify the more specific effects of the deficiency in cystine, although actual experimental data on an uncomplicated cystine deficiency would be of interest.

The experiments on the role of cystine in tumor development were next extended to the production of hepatic tumors in rats fed p-dimethylaminoazobenzene. White and Edwards (*J. Nat. Cancer Inst.* **2,** *535 (1941–42)*) employed a basal low-cystine diet containing 6 per cent casein, 25 per cent of fat, and 400 mg. of brewers' yeast per rat daily. When 0.06 per cent of the azo dye was added to the low-cystine ration, only 4 of 26 rats developed hepatic tumors in two hundred days as contrasted with the presence of tumors in 79 out of 82 animals receiving an addition of 0.5 per cent cystine in the diet. The effect of the low-cystine diet was mainly one of delaying the onset of this type of cancer; at three hundred ninety days 61 per cent of the low cystine animals had tumors as compared to 96 per cent in those fed the high cystine diet. In further studies (*J. Nat. Cancer Inst.* **3,** *43 (1942–43)*) these authors demonstrated that supplements of methionine, or of the combination of cystine and choline, were as effective in increasing the development of hepatic tumors as cystine itself, although both the methionine and the choline tended to minimize the cirrhosis frequently observed in rats fed p-dimethylaminoazobenzene.

White and Andervont (*J. Nat. Cancer Inst.* **3,** *449 (1942–43)*) have demonstrated that cystine functions in the absence of an exogenous carcinogenic agent. They employed the C3H strain of mice in which spontaneous mammary tumors develop in over 97 per cent of virgin female mice fed a standard dog biscuit. When the low cystine diet was fed (as in the leukemia experiments), no tumors developed in any of 45

animals even after twenty-two months. Forty-two litter mates fed an additional 0.5 per cent cystine exhibited a tumor incidence of 97 per cent and the tumors appeared at an average age of 9 months. This experiment is critical not only because of the profound and clearcut distinction between the results of the two groups, but also because no carcinogenic agent was administered. Hence the effect of the added cystine could not have been complicated by detoxification reactions nor by secondary debilitating effects of the carcinogen.

It was pointed out that mice on the low cystine diet averaged only 12.4 g. in weight at 6 months as contrasted with 25.3 g. for those fed the high cystine diet. The consumption of food by the two groups paralleled the difference in weight. Furthermore the mice on the low cystine diet showed irregular estrus cycles, or even complete lack of estrus. Any or all of these factors may have contributed to the prevention of the mammary tumors. But whatever the explanation, it is apparent that the lives of these particular animals were prolonged by feeding a diet that was suboptimal as judged by usual nutritional standards. Tolerable nutritional deficiencies have similarly tended to suppress the development of hepatic tumors on diets low in calories (*Nutrition Reviews* **1,** *144* (*1943*)), in biotin (du Vigneaud *et al.*, *Science* **95,** *174* (*1942*)), or in pyridoxine (Miner, Miller, Baumann, and Rusch, *Cancer Research* **3,** *296* (*1943*)). The precise relations between nutritional adequacy and carcinogenesis warrant much further study.

THIAMIN CONTENT OF PORK

Pork is recognized as an outstanding source of thiamin among natural foodstuffs. This attribute is a comparatively recent discovery which has resulted largely from the development of newer methods of vitamin assay.

Although several earlier researches indicated the exceptionally high thiamin content of pork, this fact gained wider recognition only with the reports of Mickelsen, Waisman, and Elvehjem (*J. Nutrition* **17,** *269* (*1939*)) and of Waisman and Elvehjem ("The Vitamin Content of Meat," *Burgess Publishing Co., Minneapolis, Minnesota* (*1941*)) in their summary of the nutritive value of meat and meat products. The quality of pork, in contrast to many other foods, was set in bold relief by the statement that "a pork chop, even when fried, may supply the total daily requirement of this vitamin." Later and extensive microbiologic assays by Williams and co-workers (*Univ. Texas Publ. no.* **4137** (*1941*) and *no.* **4237** (*1942*)) have confirmed the fact that few foods are comparable sources of thiamin.

In contrast to the relative concentration of other vitamin factors in various internal organs, thiamin is found in greater amounts in pork muscle than in liver, heart, or kidney. It appears, therefore, that the pig is unique among all species which have been studied, in that relatively high amounts of thiamin are normally found in pork muscle tissue. There has been no direct evidence to explain this high concentration, but it has been suggested that its presence is required by this species for the conversion of carbohydrate to fat. This conversion takes place to a marked extent in the pig, an animal which is normally fed rations predominantly rich in carbohydrates. The possibility that thiamin may be spared for the pig by ingested fat (Kemmerer and Steenbock, *J. Biol. Chem.* **103,** *353* (*1933*); Ellis and Madsen, *J. Animal Sci.* **1,** *84* (*1943*)) is also of interest.

However, there is a wide variation in pork thiamin values reported in the literature. In the assays given by Waisman and Elvehjem each of three samples of pork loin were

reported to contain approximately 11 micrograms of thiamin per gram (5 mg. per pound) and five other samples of loin showed a range of from 13.7 to 26.0 micrograms of thiamin per gram of fresh pork (6.2 to 11.8 mg. per pound). McIntire, Schweigert, Henderson, and Elvehjem (*J. Nutrition* **25,** *143 (1943)*) state that "a wide variation occurs in the thiamin and riboflavin contents of different pork carcasses."

Lane, Johnson, and Williams (*J. Nutrition* **23,** *613 (1942)*), in studying the thiamin content of the average American diet, give the following values for pork as representing the yields of thiamin expressed as micrograms per gram of raw edible portion: ham 11.81, loin chops 14.84, shoulder 10.51 (5.4, 6.7, and 4.7 mg. per pound, respectively). Berryman and Chatfield (*J. Nutrition* **25,** *23 (1943)*), in presenting a short method of calculating the nutritive value of diets, state that the more recent values for thiamin in the lean cuts of pork are approximately 1 to 2 mg. per 100 g. or 4.5 to 9.0 mg. per pound. These authors use in their work the average value 5.9 mg. per pound (13 micrograms per gram). Hewston and Marsh (*U.S.D.A. Misc. Publ. no.* **505** *(1942)*) give the thiamin value for raw pork in milligrams per pound as 6.4 for chops, 7.5 for loin, and 10.3 for lean ham. The values were derived from those presented by Booher, Hartzler, and Hewston (*U.S.D.A. Circ. no.* **638,** *(1942)*) supplemented by values reported in the literature in 1941.

While considerable progress has been made in assessing the thiamin value of pork, it is apparent that different pork cuts and pork from different carcasses may vary to a considerable extent in thiamin content. A partial explanation of these variations may be found in the work of Pyke (*Biochem. J.* **34,** *1341 (1940)*) and of Rice, Daly, and Robinson (*Abs., Div. Biol. Chem., Am. Chem. Soc., Detroit, Mich. p. 20B (Apr. 1943)*), who have shown that different muscles from the same hog carcass may differ as much as 200 per cent in thiamin content.

Miller and co-workers (*J. Nutrition* **26,** *261 (1943)*) have reported the results of feeding experiments in which it was shown that within certain limits, the thiamin content of pork tissue is dependent on the thiamin content of the feed of the pig. Three experimental groups, each consisting of 9 pigs, were fed rations in which the principal variable was thiamin. The "low thiamin" ration contained 1315 micrograms of thiamin per pound of feed, while the other two rations contained 3447 and 5761 micrograms of thiamin per pound, respectively. Peanut skins, brewers' yeast, and thiamin hydrochloride were used as the main sources of thiamin in the "high thiamin" ration. The thiamin intake of the "low thiamin" group of pigs was thought to be in excess of the suggested daily requirement. The correctness of this postulation is indicated by the fact that the animals grew as rapidly as those which received the "high thiamin" feed.

At the beginning of the feeding experiment the pigs averaged about 46 pounds in weight. On the one hundredth day of the experiment, and at weekly intervals thereafter, one pig from each experimental group was slaughtered. The length of the feeding periods varied, therefore, from ninety-nine to one hundred forty days. The average live weight for all groups at the time of slaughter was about 205 pounds. Samples were taken for analysis from the ham end of the loin, the center or middle loin, the shoulder, and the liver. Thiamin was determined by the thiochrome method.

The thiamin content of the pork from the pigs which received 3447 micrograms of thiamin per pound of feed was approximately twice as high as that from pigs on the "low thiamin" ration, which contained 1315 micrograms per pound of feed. While the average thiamin values for the high thiamin group (5761 micrograms per pound of feed) were all higher than those of the next lower thiamin group, the differences were not statistically significant in all cases.

In general, the results indicate that when the thiamin intake was 2.6 times greater than that on the "low thiamin" ration, the thiamin content of the pork tissues was approximately doubled. However, when the thiamin content of the ration was further increased, the thiamin content of pork was increased but slightly. This may be taken as an indication that the saturation point of these tissues had probably been reached. These conclusions were similar whether the values were expressed as micrograms of thiamin per gram of tissue protein or on a tissue weight basis. Hence it cannot be objected that the increased thiamin was due only to a possibly higher fat content of the tissues on the high thiamin diet.

While different assay methods for thiamin in pork are not always in agreement, it is clear, regardless of the method used, that pork stands out as a very rich natural food source of thiamin. From a purely academic point of view it will be of great interest to learn how and why the pig is superior to all other domestic animals in its ability to store this vitamin.

PREVALENCE OF VITAMIN A DEFICIENCY AND ARIBOFLAVINOSIS

The conflicting results provided by nutritional surveys make it extremely difficult for an impartial observer to form a satisfactory opinion as to the prevalence of deficiency disease. The obstacles which confront the worker who attempts to make a survey are, of course, many. Thoroughly satisfactory chemical methods sensitive enough to detect minor degrees of deficiency and simple enough to be applicable to large population groups have not yet been developed, even though promising headway has been made for several nutrients. Many of the clinical manifestations of deficiency (like cheilosis, ocular and lingual lesions) are not specific and are caused by multiple etiologic factors (*Nutrition Reviews* **1**, *72*, *116*, *194*, *327* (*1943*)). To complicate matters further, the signs frequently regress spontaneously so that improvement produced by therapy is not simple to evaluate. Investigators who undertake nutritional surveys in the face of these difficulties should win the respect of their colleagues for their earnest attempt to define the adequacy of our dietary habits. Cognizance should be taken of each study as it is reported in the hope that the accumulated results of many workers may eventually provide a clearer picture than is now available. Accordingly, there will be distinct interest in two surveys in Canada.

Pett (*Canad. Med. Assn. J.* **49**, *293* (*1943*)) studied a group of 232 people between the ages of 21 and 70 years whose occupation required them to read handwriting all day under conditions of fairly uniform lighting. Many of the subjects had complained of "eye strain." Each person kept a dietary record for one week and was examined with a biomicroscope at the beginning and end of the three month observation period for evidences of conjunctival opacities (supposedly caused by vitamin A deficiency) and of corneal vascularity (supposedly due to ariboflavinosis). It is interesting that during the week that dietary records were kept, 54 per cent had less than a recommended minimum of 10 ounces of milk daily, 24 per cent had no cheese, 93 per cent did not have three servings of vegetables daily, 51 per cent did not have a whole grain cereal during the week, and 43 per cent had less than four eggs during the period. Practically all had a serving of meat daily. More complete dietary analyses are not given in the report.

The subjects were divided by random selection into three groups: group A received 10,000 I.U. of vitamin A daily for ten weeks; group B was given a similar-appearing cap-

sule containing 3 mg. of riboflavin for a like period; and group C received the same kind of capsule filled with an inert material. Subjects were not aware that they had been divided into groups or that there was any difference in the supplements provided. The 63 persons who showed conjunctival opacities at the start and who received no vitamin A supplementation all had the same signs at the end of three months. Of 32 persons showing presumed vitamin A deficiency at the start, and receiving vitamin A therapy, 4 (or 12 per cent) lost these signs in three months. Therefore, either the treatment with vitamin A was not sufficient or 88 per cent of the treated subjects had their conjunctival opacities from causes other than vitamin A deficiency. There were 28 persons with corneal vascularization who received riboflavin. Of these, 16 had lost the signs at the end of the study, an apparent cure of 57 per cent. However, of 57 subjects with similar changes who were given no riboflavin, 24 or 42 per cent showed recovery. This high incidence of "spontaneous cures" emphasizes the importance of controls when riboflavin therapy is evaluated. Pett is very guarded in his conclusions but states that "nevertheless there remains a residue of cases diagnosed riboflavin deficiency, and responding to riboflavin treatment." He also observes that more relief of symptoms such as watery and red eyes was reported by the members of the group which was given riboflavin. However, one gains the impression from the paper that the mere presence of conjunctival opacities and of corneal vascularization among these people could not be accepted as satisfactory evidence *per se* of vitamin A deficiency or of ariboflavinosis.

Tisdall, McCreary, and Pearce (*Canad. Med. Assn. J.* **49**, *5 (1943)*) were stimulated to study the incidence of corneal vascularity among men in air crews of the Royal Canadian Air Force because riboflavin is destroyed by light, and air crews are exposed to much more light than is commonly encountered in civilian life. The authors thought it possible that this increased exposure might bring about increased destruction of riboflavin in the eye, and hence increase requirements. Furthermore, assays of the R.C.A.F. rations as served prior to June 1, 1942, averaged only 1.6 mg. of riboflavin daily in contrast to the frequent recommendations of 2.5 to 3.0 mg. In order to make their study as objective as possible, photographs of the eyes were made at intervals of two weeks and their report is beautifully illustrated with remarkably clear photographs. With respect to vascularization, a normal eye was defined as one in which no proliferation of the vessels was present. They recognized three stages of corneal vascularization. In stage I there was proliferation of the vessels of the limbic plexus with either no penetration of the cornea or penetration only with tiny twigs in one or two sharply defined areas. With stage II, there was penetration of the cornea with twigs and streamers. In stage III, the corneal penetration included loops of vessels. One hundred and ninety-eight men examined in May, 1942, showed changes which caused them to be classified as follows: "normal eye, 1 (0.5 per cent); stage I, 17 (8.6 per cent); stage II, 87 (43.9 per cent); and stage III, 93 (46.9 per cent)." Seventy of the men in stage III were chosen for an evaluation of the effects of treatment with riboflavin. Sixty-seven per cent of these suffered from two or more of the following symptoms: tiredness of eyes, aching of eyes, watering of eyes, sandy sensation under the lids, dizziness, headaches, reading intolerance, decreased visual acuity. Usually these symptoms were worse after flights in bright weather, or occurred only at these times. The men were divided into three groups: one received 3.3 mg. riboflavin (3x) daily for two months, the second received the same supplement for one month only, and the third was given capsules similar in appearance but containing no riboflavin. Of the 28 subjects who received 9.9 mg. of

riboflavin daily for two months, 20 or 71.4 per cent showed either marked or moderate improvement in the extent of vascularization. Eight of the men showed slight, doubtful, or no improvement; an increase occurred in none. Of the 21 men who were given treatment for one month, 6 (28.6 per cent) showed marked or moderate improvement, 14 (66.6 per cent) had slight or doubtful improvement or no changes, and one man showed an increase in vascularity. Among the untreated 21 subjects, none showed marked or moderate improvement, 15 (71.4 per cent) were either unchanged or showed doubtful improvement, and 6 (28.6 per cent) were worse. When improvement occurred with therapy, it was gradual over the two months' period of observation. Little change was observed during the first two weeks of therapy and in only one case was there marked change within two weeks.

The therapeutic results obtained by Tisdall and associates were well controlled and data were made objective by the use of photographs of the eye. It is reasonable, however, to question a classification based on anatomic evidence which permits only one young man out of 198 presumably healthy persons to be classified as "normal." The majority of subjects with grade III changes seemed to respond to riboflavin administration. One wonders, however, whether the response among men in groups I and II would have been nearly as good. Possibly the slighter degrees of corneal vascularization present in them were not caused by ariboflavinosis. That 99.5 per cent of these men had clinically evident manifestations of deficiency disease is almost inconceivable. Certainly in Pett's subjects corneal vascularization was not so consistently a sign of riboflavin deficiency.

PANTOTHENIC ACID AND THE GASTROINTESTINAL TRACT

Dogs made deficient in pantothenic acid frequently develop gastritis or enteritis and intussusception (Schaefer, McKibbin, and Elvehjem, *J. Biol. Chem.* **143,** *321 (1942)*). Hypoglycemia may also occur and may be severe enough to cause coma. While the low blood sugar values can be explained readily by the attendant severe hepatic degeneration and probable absence of liver glycogen, it is possible that poor absorption of carbohydrate is also partly responsible. There is need, therefore, for further elucidation of the function pantothenic acid plays in the physiology of the gastrointestinal tract. Valuable information of this type has been supplied by Bly, Heggeness, and Nasset (*J. Nutrition* **26,** *161 (1943)*).

These workers studied the effects of pantothenic acid and of inositol on the motility, digestion, and absorption in the upper intestinal tract of dogs. The 2 animals used for the experiments were adults on whom jejunostomies had been established about 50 cm. distal to the ligament of Treitz. During the period used for the performance of control observations, a basal diet of casein, sucrose, hydrogenated vegetable oil, bone ash, dried brewers' yeast (10 per cent of the ration), and salts was fed. The experimental ration consisted simply of fresh bread made from peeled whole wheat; about 400 g. per day were consumed by each dog. The vitamin content of the bread in micrograms per gram was as follows: thiamin, 2.73; riboflavin, 2.45; pyridoxine, 3.14; pantothenic acid, 5.2; inositol, 644; and niacin, 30. Supplements of the fat soluble vitamins were provided during all periods. A severe deficiency of pantothenic acid was produced in two or three months when dogs were fed the experimental diet. Chyme was collected in the following manner: a two-lumened catheter with a rubber balloon on the end was passed through the

fistula into the lumen of the gut, the balloon was inflated through the smaller lumen with approximately 10 ml. of air, and chyme was gently aspirated through the larger lumen. Each half hour the enzymatic activity of the collected chyme was inactivated by heat. The fasting (twelve to twenty hours) dog was given a test meal of 100 g. of the thoroughly dried bread suspended in 250 ml. of water. Motility of the intestinal tract was measured by determining the length of time required for all of the test meal to be cleared from the upper intestinal tract. Analyses were made on the test meal and on the chyme for reducing sugar, total carbohydrate, diffusible and total nitrogen. From these data were calculated the amounts of carbohydrate and protein which had been digested and absorbed.

The emptying time was lengthened from the normal time of about six hours to between ten and twelve hours during pantothenic acid deficiency periods. Addition of 220 micrograms of calcium pantothenate per kilogram per day restored the motility to normal. The promptness with which this change occurred is not clear from the data provided, but in one comment the authors state that "the emptying time dropped to a normal average of 5.6 hours over a period of a month." Since deficiency resulted with the experimental diet which provided daily approximately 130 micrograms of pantothenic acid per kilogram of body weight, and since an additional 220 micrograms per kilogram corrected the deficiency, the dog's requirement is probably between 130 and 350 micrograms per kilo per day. Furthermore, digestion and absorption of carbohydrate and protein were 40 to 60 per cent less during the deficient than during the control periods. Pyridoxine administration was ineffective in altering the course of the deficiency. Inositol given subcutaneously (up to 33 mg. per day) had no effect, but when it was given orally in amounts as great as 500 mg. per day it temporarily increased motility but decreased digestion and absorption. Its effect, therefore, was more like that of a cathartic. The experiment was complicated by the fact that after five or six months a salt deficiency also appeared. At this time pantothenic acid was less effective in restoring and maintaining normal gastrointestinal function unless a salt supplement was also given.

In contrast to these results which emphasize previous data that pantothenic acid is important to the normal functioning of the intestinal tract, are those obtained by Leonards and Free (*J. Nutrition* **25,** *403 (1943)*). These workers studied the effect of pantothenic acid on the absorption of galactose in rats. One member of each pair of litter mate rats, fed a synthetic ration deficient in pantothenic acid, was given a supplement of 100 micrograms of calcium pantothenate daily. The absorption experiments were done after animals has been on the experimental diet for seven to nine weeks. A test dose of galactose was then given and the animals sacrificed at the end of one hour. The amounts of galactose remaining in the stomach and intestines were determined, as well as the concentration in the blood. No significant difference was observed in the blood levels of galactose for deficient and control animals, but the amount of galactose which had been absorbed from the intestinal tract was 15 per cent greater in the pantothenic acid supplemented rats than in those that were deficient. In other experiments, it was determined that the addition of 300 or 1000 micrograms of calcium pantothenate daily to an adequate stock diet did not detectably influence the absorption of galactose.

While Leonards and Free, therefore, detected some effect of pantothenic acid on absorption, the effect was much less definite than in the studies by Bly and associates. Part of the difference may be related to the fact that galactose does not need to undergo any digestion before it is absorbed. It is not clear, therefore, whether pantothenic

acid, in addition to influencing motility, functions by regulating absorption, digestion, or both. Since Bly's results were obtained in only 2 animals, final acceptance of his physiologic observations must be withheld until confirmation is provided.

INTERRELATIONS BETWEEN THYROID FUNCTION AND VITAMIN METABOLISM

There is considerable interest from both a theoretical and a practical viewpoint in possible relationships between vitamins and hormones. Similarities between these two groups of biologically active substances have been frequently pointed out. Both produce highly specific effects at very low concentrations. Indeed it might appear, superficially at least, to be merely a question of source, the vitamins being obtained from food, the hormones from specialized tissues. Even this difference appears to vanish in certain cases. Ascorbic acid, for example, although required in the diet of some animals (man, monkey, guinea pig), is synthesized by the tissues of most others. Likewise dehydrocholesterol is synthesized, perhaps by the liver, and irradiated in the skin to become a D vitamin produced within the organism itself.

There is, of course, a more fundamental difference between vitamins and hormones than their place of origin. According to a widely held concept the vitamins furnish difficult-to-produce parts of the essential chemical machinery of the organism, whereas the endocrines regulate this machinery. Because of this theoretical relationship the manipulation of the amounts of both vitamin and hormone available to the organism should represent a valuable experimental procedure.

The extensive studies that have been made on the interrelations between vitamins and the thyroid gland and its secretion have been reviewed by Drill (*Physiol. Rev.* **23,** *355 (1943)*). These interrelationships are of great theoretical interest since both the vitamins and thyroglobulin are deeply involved in energy metabolism. Furthermore the prevalence of disturbances of the human thyroid gland makes it important to know the effects of deranged thyroid function on vitamin requirements as well as any possible benefits which might be derived from unusual vitamin intakes.

It is many times more difficult to establish relationships between two biologically active materials than it is to explore the effects of either one of them alone on the organism, since there is an almost infinite variety of experimentally possible combinations of concentrations and timing of administration. It is therefore not surprising that apparent contradictions arise in the literature, and that in spite of a vast amount of work, but few substantial conclusions may be drawn. Presumably many of the contradictions arise from differences in technic, concentrations of the substances employed, and duration of the experiments.

The possible interrelationships may be classified according to (a) the effects of hyperthyroidism or hypothyroidism on vitamin requirements; (b) the effects of vitamins on hyperthyroidism or hypothyroidism; and (c) the effects of vitamins on the thyroid gland itself and on the thyrotropic hormone output of the pituitary.

It is not possible to mention in this brief review all of the data summarized by Drill. Some of the findings are intricate and particularly controversial. For these the reader is referred to the original review.

There is general agreement that hyperthyroidism increases the requirements for several of the vitamins, e.g., vitamin A, thiamin, pantothenic acid, pyridoxine, and ascorbic acid. This is particularly well documented in the case of thiamin. In-

creased metabolism and excretion have been held responsible for the increased requirement of some of the vitamins. There may be sufficient liver damage in hyperthyroidism to interfere with the metabolism and storage of vitamin A.

One difficulty in establishing the vitamin requirement in experimental hyperthyroidism is that weight curves are the most common criteria of vitamin sufficiency and an excess of thyroid hormone *per se* will adversely affect the growth curve.

It has become reasonably well established that thiamin requirements under ordinary circumstances are directly proportional to the carbohydrate utilization and hence, with a diet of uniform composition, proportional to the total metabolism. Although clearcut evidence is not presented, one gains the impression that the increase in utilization of thiamin in hyperthyroidism exceeds the increase in metabolism. The maximum amount of thiamin which the liver will retain is reported to be lowered in hyperthyroidism. Although an increase in thiamin excretion has been reported, the magnitude of the increase would represent perhaps only 10 per cent of the daily requirement. This increase appears to be chiefly the consequence of a marked diuresis.

The tachycardia of hyperthyroidism may be prevented, in dogs at least, by withholding thiamin from the diet. This seems to be the result of superimposing the bradycardia of thiamin deficiency onto the tachycardia of hyperthyroidism so as to produce an apparent neutralization.

It is exceedingly interesting that there is no report of any increased demand for riboflavin in hyperthyroidism. It has yet to be established that the requirements for riboflavin bear any relation to the total metabolism.

There are a number of clinical reports of abnormally low serum vitamin A and carotene concentrations in Graves' disease. Administration of vitamin A failed to produce the rise in serum vitamin A observed with normal persons. Following successful treatment with iodine or surgery the serum values for vitamin A were increased (Wendt, *Klin. Wchnschr.* **14,** *9 (1935)*; *München. med. Wchnschr.* **82,** *1160 (1935)*).

Experimental hyperthyroidism, in laboratory animals, produces a fall in vitamin A and carotene in the liver, but in contrast with this, livers removed at autopsy from patients with Graves' disease have been found to contain somewhat higher than normal amounts of vitamin A. Unfortunately the evidence in experimental animals for an increased requirement of vitamin A as a result of hyperthyroidism is incomplete. Fasold and Peters (*Ztschr. f. d. ges. exp. Med.* **92,** *57 (1934)*) made the interesting claim that the ill effects of huge doses of vitamin A are overcome by thyroxin.

There is some evidence that the requirement for ascorbic acid in the guinea pig increases after thyroxin administration. It is perhaps even more interesting that in both the dog and the rat, which ordinarily do not require ascorbic acid, a decrease has been observed in the tissue ascorbic acid concentration as a result of thyroxin administration.

Possible changes in vitamin requirements as a result of hypothyroidism have received less attention than have those changes in requirements resulting from hyperthyroidism. A seemingly significant finding that has been rather well confirmed is that there is little or no conversion of carotene to vitamin A in thyroidectomized animals or hypothyroid patients. There are several lines of evidence: (a) the milk of goats which is normally rich in vitamin A becomes, instead, rich in carotene after thyroidectomy; (b) xerophthalmia has been induced in thyroidectomized rabbits on diets which contain sufficient carotene to protect normal animals; (c) the condition of carotenemia, in which sufficient carotene accumulates in the blood to give a yellow appearance to the skin, is apparently observed only in

patients who convert carotene to vitamin A at a less than normal rate. A number of such persons have been reported to be thyroid deficient, whereas others have had some type of liver damage. The carotenemia in hypothyroidism may likewise be due to liver damage although in many instances the liver damage, if it exists, is too mild to be demonstrated by other criteria.

These are the effects of thyroid hormone on vitamin metabolism. The vitamins in turn may possibly affect the action of the thyroid hormone. Much attention has been directed to alleviating the ill effects of Graves' disease through improvements in the diet. To the extent that vitamin requirements are increased, additional vitamin supplements should of course help. However, there is considerable doubt as to whether any improvement beyond this occurs. A number of authors report that thyroxin induces less of an increase in the basal metabolic rate when either vitamin A or carotene is given concurrently. Once, however, the basal metabolic rate has been raised by thyroxin acting alone, vitamin A administration is said to be no longer effective. Ascorbic acid in large amounts has also been reported to lower the basal metabolic rates in hyperthyroid rats.

Hyperthyroid dogs eventually show a decreased liver function as measured by bromsulfalein. Drill, Shaffer, and Overman (*Am. J. Physiol.* **138,** *370 (1942–43)*) found that the average time required to produce demonstrable liver damage was decreased from ninety to twenty-two days by removal of the B-vitamins (yeast) from the diet. Although not definitely proved, this is probably due to the result of an increased destruction of thiamin and other vitamins of the B-complex in hyperthyroidism. It is interesting to compare this protection from thyroxin with the protection of the liver by yeast against choloroform, butter yellow, and other toxic substances.

Hyperthyroidism may lead to a negative calcium balance. Vitamin D in proper dosage has been reported to restore the calcium balance. Other descriptions of improvements, in hyperthyroid animals, from various vitamins may be merely a cure of a mild vitamin deficiency induced by the hormone excess rather than any specific antagonism between hormone and vitamin.

Under certain circumstances several different vitamin deficiencies may lead to hypertrophy of the thyroid gland. One may speculate on the possibility that this response by the thyroid to the deficiency represents a compensatory mechanism tending to overcome the ill effects of the vitamin deficiency. Curiously, it has been found that vitamin A deficiency produces hypertrophy of the thyroid in the female rat but atrophy in the male, and this illustrates the complexity of the interrelationships involved. Hypervitaminosis A also affects the thyroid, but unfortunately the results are discordant.

In summary it seems clear that (a) the requirements for certain vitamins are increased by hyperthyroidism; (b) hypothyroidism in some way interferes with the conversion of carotene to vitamin A; and (c) under certain conditions the thyroid may become hypertrophic as a result of deficiency of several different vitamins. In addition, there are a variety of less clearcut interactions which, while somewhat obscure, must certainly not be dismissed too lightly. Some of the effects reported are difficult to explain on the basis of an increased destruction or excretion of the vitamin in hyperthyroidism. These are perhaps the most interesting effects and may furnish clues as to the mechanism by which thyroglobulin exerts its effect. It seems clear that the interrelationships between vitamins and hormones deserve a more thorough exploration.

VITAMINS FOR GRAY HAIR

The application of the newer knowledge of the vitamins to man has seemed such a simple matter that even certain lay persons and organizations have taken it upon themselves to carry on investigations and to give instruction to the public as to the value of vitamins for various purposes. Untrained individuals, unfortunately, usually do not appreciate the necessity for adequate control and painstakingly accurate observations in experimental studies. As a result the public may be misinformed and misled. A recent example is the publicity which has been given to the supposed restoration of color to gray hair by the use of calcium pantothenate. Certain popular magazines, newspapers, and misleading advertisments appearing in drugstores have claimed that calcium pantothenate is an effective agent in restoring "the original color to the hair." These claims derive from well founded observations in rats and certain other animals receiving artificial diets but adequate clinical evidence has never been offered.

Critical observers appreciated from the first that it was not probable that the aforementioned experimental observations would be applicable to man. It has not yet been determined that the human diet is deficient in pantothenic acid as a single factor or even that pantothenic acid deficiency occurs in man. Furthermore, the production of graying has been accomplished only in young animals, not in full grown ones. The claims concerning the effects of calcium pantothenate in man have referred to adults.

A careful clinical study has been reported by Kerlan and Herwick of the Food and Drug Administration (*J. Am. Med. Assn.* **123,** *391 (1943)*). These observations were carried out for a six month period on 21 white women and 6 white men ranging in age from 34 to 62 years. Two white women and 4 white men between 29 and 62 years of age served as controls.

The subjects of these experiments represented degrees of decrease of hair pigment varying from beginning graying to "all white." Loss of hair color had been present in all but one instance for ten years or longer. In the one exception rapid graying had occurred in the past three years. All of the subjects were government employees who could afford and did have adequately varied diets.

Each experimental subject took 2 tablets of calcium pantothenate, furnishing a total of 20.4 mg. per day. The tablets were taken under the supervision of the investigators. In order to make the study as objective as possible, color analyses were made of samples of hair which were collected before, during, and at the close of the experiment. The samples were obtained from the men by collecting the hair cuttings. In the women, samples of hair from representative areas of the scalp were obtained and as the hair regrew the area was recut to furnish samples for comparison with the original sample of hair cut shortly before the patient began taking calcium pantothenate. The color determinations were made by an expert in the field of color analysis.

The observations revealed no change in hair color whether examined clinically or by expert color comparison. Several persons in the age group of 34 to 40 years felt that there was an increase in hair grayness. In several instances friends remarked to the subjects that they could see a "darkening" in the color of the hair but the users themselves were unable to detect any change and color comparisons revealed no change. In one woman a "yellowing" effect was noted in the free ends of an isolated white strand of her hair.

These findings are consistent with those of Brandaleone, Main, and Steele (*Proc. Soc. Exp. Biol. Med.* **53,** *47 (1943)*), and of Vorhaus, Gompertz, and Feder (*Am. J. Digest. Dis.* **10,** *45 (1943)*), who also were unable

to detect any effect of calcium pantothenate on the gray hair of human beings. It does not necessarily follow from these observations that in the human individual graying of the hair is never caused by a lack of pantothenic acid. Observers, however, have yet to find such a case. The extravagant claims which have been made for calcium pantothenate in relation to graying hair in man have no foundation.

PROBLEMS OF FEEDING INSTITUTIONAL AND INDUSTRIAL WORKERS

In industrial and institutional feeding programs, menu planning, kitchen management, food preparation, and service must be properly integrated if the goal of adequate nutrition for the worker is to be attained. One of these factors which has been investigated recently is that of food preparation and service. In view of the dearth of information concerning the losses of nutrients in food prepared in industrial and institutional cafeterias, the reports of the vitamin content of vegetables as served to the customer are of interest. The study from Cornell University by Heller, McCay, and Lyon (*J. Nutrition* **26,** *377 (1943)*) was conducted at one of the cafeterias feeding approximately 2500 workers in the Brooklyn Navy Yard. The purpose of this study was to give a rough estimate of the total losses of vitamins in the actual field of large scale cookery rather than to present a carefully controlled study to locate the steps in the cookery that cause the losses.

Carotene, ascorbic acid, riboflavin, and thiamin were determined. The exact losses of these vitamins in different stages of preparation of the vegetables were not determined, but the over-all percentage loss was as follows: thiamin 16 to 64; niacin 2 to 61; riboflavin 22 to 45; ascorbic acid 27 to 90. Changes were then made in the vegetable cookery by decreasing radically the time of cooking large quantities. The time of holding vegetables between cooking and service was also reduced to a minimum; unfortunately vitamin losses were not redetermined with these possible technical improvements.

The authors have prepared a table to show which vitamins and how much of the various vitamins the customer actually received from a serving of vegetables obtained in the cafeteria. The size portion of one serving of all vegetables except potato was 85 g. A serving of potato was 112 g. Green lima beans, green string beans, spinach, and green peas were frozen products; fresh cabbage, potatoes, carrots, and turnips were used. As shown in the table, the outstanding sources of carotene were spinach and carrots, the former containing 7450 I.U. and 8216 I.U. in two samples, and the latter 9605 I.U. in one sample.

Two samples of peas supplied 150 micrograms and 220 micrograms of thiamin per serving. Four samples of potatoes were found to contain between 80 and 100 micrograms of thiamin. Lima beans, green beans, spinach, cole slaw, carrots, and turnips supplied between 30 and 60 micrograms per serving. The riboflavin values of all vegetables were found to range between 20 and 80 micrograms per serving. The niacin content of all vegetables was between 0.13 and 0.77 mg. except for peas which were found to contain 1.45 mg. per serving. The ascorbic acid content of most of the vegetables was between 1.1 and 7.8 mg. per serving. However, spinach which had not been defrosted before cooking contained 14.5 mg. per serving.

It is of interest to compare these ascorbic acid values with those obtained by Daum, Aimone, and Hollister (*J. Am. Dietet. Assn.* **19,** *693 (1943)*) who studied the ascorbic acid content of similar vegetables prepared in an institutional cafeteria serving 1400 individuals. Even though certain vegetables

were canned instead of frozen as in the above study, similar results were obtained. The values for spinach, peas, string beans, cabbage, carrots, and potatoes after cooking and holding were 1.7 to 8.5 mg. of ascorbic acid when compared on the same per serving basis as mentioned previously. Additional vegetables were studied by Daum and associates. Asparagus, cauliflower, sauerkraut, and tomatoes were found to contain 9.4 to 14.5 mg. of ascorbic acid per 85 g. serving. These workers also found that a greater loss in ascorbic acid occurred due to holding of vegetables on the steam table for one hour than occurred in the cooking, with the exception of cabbage and sauerkraut. In order to maintain the holding time at a minimum, preparation in the kitchen was staggered for many of the items, particularly the potatoes.

Heller, McCay, and Lyon have pointed out that other schemes which help speed service and reduce holding time are: (1) posting menus in large print in strategic places so that the customer can make his choice before he gets to the counter; (2) decreasing daily choice as much as possible, since adequate choice can be extended over a period of time in the menus; (3) making the main dish choices as distinct from each other in appearance, flavor, and cost as possible, to avoid confusion and indecision. Decreasing choice aids in kitchen management. Preparation of fewer items simplifies the kitchen schedule, improves the work of untrained help, and increases the efficiency in use of limited equipment.

Another factor which must be considered in attempting to raise the level of vitamin intake is that of menu planning. Food items which will improve the level of vitamin intake should be used. In addition, recipes can be adapted to the use of foods potent in valuable nutrients. Soybean products and dried yeast have been found acceptable for this purpose. Heller, McCay, and Lyon (*J. Nutrition* **26,** *385 (1943)*) have incorporated yeast in their large scale recipes and found that it proved a satisfactory method of supplementing the levels of vitamins. The yeast was usually added to the meat dishes at conservative levels so that the taste was not detected. Since yeast is rich in protein of good quality it also affords a good source of this dietary factor. With the recent development of mild flavored yeast this addition will probably become more generally acceptable. Other little used foods of high nutritive value may well be exploited with a view to incorporation in institutional and industrial cookery.

In striving to reach the goal of adequate nutrition for the worker, it is important to note that while consideration can well be given to the conservation of vitamins in vegetables by improvements in preparation and service, the factor of menu planning can be of relatively greater significance in providing the recommended vitamin allowances.

NUTRITION IN PREVENTIVE MEDICINE

Nutrition is assuming a place of increasing importance in preventive medicine. However it is unfortunate that preventive medicine is given such a minor part in medical teaching today. Certain studies have suggested that mild degrees of deficiency may have importance in producing symptoms, the causes of which were hitherto unrecognized. Some even argue that the importance of nutritional deficiencies is indicated by the fact that so many practicing physicians are prescribing vitamin preparations. The significance of such evidence as indicating the extent of nutritional deficiency may be questioned, but that this is an important problem no one will deny.

The factors which lead to development of nutritional deficiencies are varied and it is important to recognize that poverty is not the only one. Goodhart (*J. Am. Med. Assn.* **121,** *93 (1943)*) has shown that as much as 90 per cent of the thiamin present

in fresh raw food was lost before the food was eaten, as a result of poor preparation, overcooking, and keeping the food hot for long periods of time. Other factors include idiosyncrasy, food fads, gastrointestinal disorders, and increased metabolic requirements.

It would be helpful to have accurate information as to the extent and degree of nutritional deficiencies in various localities. Such information is not yet at hand because it requires accurate methods of assay as well as knowledge of the significance of deviations from arbitrarily set normals. In a later review, however, Sebrell (*J. Am. Med. Assn.* **123,** *280, 342 (1943)*) has brought together the statistical data which have been reported and they are listed in convenient tabular form.

Interpretation of these data is difficult. According to these studies, vitamin A deficiency has been found in from 9 to 83 per cent of the subjects examined in India and in China, respectively. Where xerophthalmia and keratomalacia serve as the criteria of vitamin A deficiency, reliance can be placed on the observations. Where night blindness is the criterion, one is much less certain of the results as this symptom may be caused by factors other than vitamin A deficiency. One wonders, for example, about the significance in regard to vitamin A deficiency of the finding of night blindness in 45 per cent of 500 schoolchildren in Venice.

Where vitamin deficiency is concerned, it is doubtful whether the prevalence of beriberi may be taken as an indication of the extent of thiamin deficiency. Thiamin deficiency, undoubtedly, is much more common than would be indicated by the incidence of beriberi. Yet it is impossible to judge by such symptoms as loss of appetite, lassitude, and unusual fatigability which may occur under many circumstances other than thiamin deficiency.

The statistics which Sebrell has collected include the well known high incidence of pellagra in the Southern states and give interesting figures for other countries. These data give some conception of the frequency of nicotinic acid deficiency although pellagra represents a severe and often in reality a multiple deficiency disorder. Ariboflavinosis is frequently present at the same time.

The significance of certain signs which have been described as indices of ariboflavinosis is questioned by some authorities. If corneal vascularization and cheilosis are valid criteria, then this is the most common type of deficiency in the United States. In a study by Wiehl and Kruse (*Milbank Memorial Fund Quart.* **19,** *241 (1941)*) as many as 75.8 per cent of the pupils in a school in the east side of New York City had signs which were attributed to riboflavin deficiency.

Blood levels of ascorbic acid below those given as normal or optimal are found frequently. How low these must fall before one should attach serious significance to them is a moot point. There is no doubt, however, as Sebrell's statistics indicate, that scurvy is prevalent in certain parts of the world.

Whatever the exact figures may be, everyone agrees that a problem exists in the prevalence of nutritional deficiency, the correction of which should have an important bearing on the health and efficiency of the people of the world. It is also becoming evident that the total production of food is only one factor in meeting this problem. An equally important factor is the development of national food habits and policies for the entire population. It is clear that health and medical authorities must assume more of the burden of solving nutritional problems.

DIET AND EXPERIMENTAL HEPATIC TUMORS

Nutritional factors unquestionably alter the carcinogenic effect of p-dimethylaminoazobenzene in producing hepatic tumors in rats (*Nutrition Reviews* **1,** *247 (1943)*).

The tumors develop more readily when animals are fed certain deficient diets. Addition of protective foods to the rations decreases the carcinogenic activity of the azo dye and lowers the incidence of tumors. Foods known to be partially protective are liver, yeast, milk, rice, and extracts or concentrates of these materials. A mixture of casein and riboflavin has a similar action but either substance alone fails to influence the development of tumors. When biotin is added to protective diets, their protective value is lost (*Nutrition Reviews* **1,** *280 (1943)*).

These results seem definite enough even though no adequate explanation for them has yet been found. That they may be complicated by another factor, however, seems likely from studies by Hanszen and Selle (*Proc. Soc. Exp. Biol. Med.* **54,** *225 (1943)*) which demonstrate that the relatively indigestible portions of yeast, liver, and rice bran adsorb considerable amounts of p-dimethylaminoazobenzene from aqueous solutions *in vitro*. This observation led Hanszen and Selle to set up an experiment designed to determine whether the protective action of any of the foods might be due to adsorption of the azo dye and consequent poor absorption of the carcinogenic dye from the intestines. Montmorillonite, a riboflavin-free, indigestible, nontoxic adsorbent clay, was selected for inclusion in the ration. Forty young rats of the Wistar strain were divided into two groups similar in number, age, sex, and weight. Both groups were fed for one hundred seventy-five days a basic carcinogenic diet containing the amount of the dye used by Sugiura and Rhoads (*Cancer Research* **1,** *3 (1941)*) in their experiments. The treated group was given one part (by weight) of montmorillonite per ten parts of the basic ration. Eighteen of the 20 control animals but only one of the montmorillonite-fed rats developed hepatic tumors during the experimental period. No evidence of marked vitamin deficiency appeared in either group. The experimental animals, however, gained only about two-thirds as much weight as did the controls.

These experiments are reported as preliminary observations. They certainly demonstrate that inclusion of an adsorbent clay in a carcinogenic diet containing p-dimethylaminoazobenzene lowers the incidence of hepatic tumors produced in rats. Interpretation, however, must be made with extreme caution or be withheld until further results have been obtained. The animals ingesting the clay were said to excrete 53 per cent less p-dimethylaminoazobenzene in the urine than those not receiving the clay; the actual amounts involved were not published. Ordinarily when carcinogenic amounts of azo dyes are fed to rats, less than 1 per cent of the amount ingested appears in the urine as an azo compound. It is, therefore, questionable how much significance should be placed upon a further reduction by 53 per cent. No evidence was presented of an increased excretion in the feces by the rats fed clay. Furthermore 10 g. of the water insoluble portion of unpolished rice flour, rice bran, dried beef liver, and dried brewers' yeast, for instance, adsorbed only 4 to 9 mg. of the dye *in vitro* while a similar amount of montmorillonite adsorbed from 472 to 954 mg. It does not necessarily follow, therefore, that the protection afforded by these foods is similar in kind to that of the clay. One also wonders if montmorillonite adsorbs biotin so that a relative biotin lack might operate to decrease the incidence of hepatic tumor formation. Finally, evidence must be offered to show that simple reduction by approximately 53 per cent of the dye added to rations will reduce tumor formation to a similar degree before the effect of the clay can be assigned to its dye-adsorbing properties alone. It is difficult, furthermore, to correlate the adsorption theory with the demonstrated protective action of riboflavin.

NOTES

Letters to the Editor

Dear Sir:

Let me congratulate you on NUTRITION REVIEWS. Some kind friend had seen to it that my name was placed on your mailing list, so when I arrived on the GRIPSHOLM I found a complete file beginning with volume 1, number 1, awaiting me. Your publication is filling a real need. We were issuing in Peking a little publication for China called "Nutrition Notes" which had about the same objective. Our twelfth issue was about to go to press when the opening of hostilities in the Far East put a stop to all such activities. . . .

Very truly yours,
William H. Adolph,
Professor of Biochemistry,
Yenching University,
Peking, China.

Dear Sir:

I would call to your attention certain uncritical observations in your article on the "Nutritive Value of Dehydrated Vegetables" p. 393–4 of your November issue.

It is stated that there is an 80 per cent loss of carotene in carrots on drying, and as much as 90 per cent in spinach. I call to mind the early preparative work of Smith (*J. Biol. Chem.* **96,** *36 (1932)*) where carrots are dehydrated and extracted to give yields of *recrystallized* carotene of 1.4 g. per 1.67 kg. carrot powder. Similarly, on p. 38, the method is described for preparing carotene from dehydrated green leaves. It will be noted that the carrots were given a mild water blanch, whereas the leaves were not.

The fact remains that dehydrated carrots, prepared industrially, do not show losses of the magnitude indicated. In your citation of the work of DeFelice and Fellers, you fail to point out, as they would be the first to admit, that this material was dried in 1937, that it is not indicated that the sample had been blanched prior to dehydration, that presumably it was stored for three months (see their table I) probably not in inert gas, and at an unstated temperature, presumably that of the room.

There may be, among old-timers, some divergence of opinion as to blanching of cabbage, but both from the standpoint of industrial production and storage, even at 70–80°F., there is no question as to its desirability, and as for carrots, it is absolutely essential, if carotene is to be retained. The statement therefore on p. 393 that carrots should be dehydrated without blanching is simply not in accord with the facts.

It is unfortunate that in dealing with losses of ascorbic acid, your commentator did not draw on the papers by Cruess and Joslyn, and by Chace, in the Proceedings of the Inst. of Food Technology (1942). The effect of moisture content on storage is of utmost importance. Your omission of reference to the recent work of Zscheile on the proportion of beta carotene to other isomers in certain green vegetables is also regrettable. (*see Nutrition Reviews* **1,** *187 (1943)—Ed.*)

Very truly yours,
G. Mackinney,
University of California,
College of Agriculture,
Berkeley, California.

Dear Sir:

. . . The one point which I like best of all is that most of the reviewers indicate what they think is the significance of the work reviewed. Of course everyone understands that it is their own opinions but that is exactly what we want in reviews. Furthermore they often indicate further problems

of importance related to the work. That is extremely valuable for the young workers. . .

Very truly yours,
Walter J. Meek,
Professor of Physiology,
University of Wisconsin,
Madison, Wisconsin.

Dear Sir:

In the interest of accuracy of reporting may we bring to your attention an inconsistency in one of your recent review articles? In the November issue (**1,** *403 (1943)*) under "Thiamin inactivation by raw fish" you introduce Sealock's studies with the statement that "they first developed a chemical assay method for the factor" and then indicate that the fermentation method for thiamin was used. Actually the authors in the original article state, "Since a chemical method would permit a greater number of determinations in a given period, the colorimetric diazonium method described by Melnick and Field was adopted for subsequent experiments." The findings presented in your review were obtained by the colorimetric method. Only for the preliminary tests was the fermentation method employed.

It may have been of some interest, since methods are generally mentioned, to have indicated that Woolley working in this particular field, also used the colorimetric method as well as a microbiologic technic for the assay of thiamin.

Very truly yours,
Bernard L. Oser,
Food Research
Laboratories, Inc.,
Long Island City, New York.

Primitive Methods of Dehydration

In view of the current concern with dehydration of various foods, it is of interest to recall some dehydrated foods employed by primitive people. Best known are pinole and pemmican widely used by American Indians. Both are durable, light in weight, and readily prepared without cooking. Pinole is made of corn or other cereal seeds, wild or cultivated. The seeds are parched and ground several times over until a fine meal is produced which is readily transported. When mixed with hot or cold water it yields a porridge or gruel which seems very sustaining. It could also be mixed with meat or fish broths or maple syrup. Occasionally the dry meal was mixed with water and dried into wafer breads or cakes.

To make pemmican, buffalo meat was cut into thin strips, dried and smoked and pounded into a powder. This was mixed with melted fat and (sometimes) dried berries or currants and allowed to solidify, thus forming a durable and compact food supply used by most American Indians. It was often mixed with water and flour to yield a thick soup. Some tribes made use of a fish pemmican in which boned, dried fish was powdered and mixed with burned flour. North American Indians, like most primitive peoples everywhere, were well acquainted with the practice of sun-drying or smoking all kinds of meat and fish. Even fish roe, octopuses, and molluscs were sun-dried as were also earthworms and many kinds of insects, either in larval, papal, or adult forms. Drying and smoking were popular means of food preservation in ancient times; salting in brine was also practiced, but not in America.

No doubt some putrefaction occurred in the process of drying meat. One might think that such a condition would act as a deterrent to its widespread use. Yet in reality the reverse often seems to have taken place. Primitive man made the best of the situation and developed a liking for such "high" meat even to the extent of preferring it to plain meat. Some people's taste in cheese runs along similar lines.

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The Nutrition Foundation was organized by food and related manufacturers to develop and support a comprehensive research and educational program in the science of nutrition. It functions chiefly through grants in support of research in university centers where there are strong graduate schools in the basic sciences. Nutrition problems of immediate importance in relation to the war emergency receive special consideration.

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